Hepatotoxicity From Bodybuilding Supplements Rising

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WASHINGTON, DC — Hepatotoxicity related to herbal and dietary supplements appears to be on the rise in the United States, and bodybuilding supplements are the most common cause, a new study has found.

"Dietary supplements aren't categorically and uniformly safe with regard to the liver. It's very difficult to identify which supplement could cause injury, so you have to assume that all supplements have the potential to cause injury," said Victor Navarro, MD, from the Einstein Healthcare Network in Philadelphia.

The data are the latest to come from the Drug-Induced Liver Injury Network, an 11-center registry funded by the National Institute of Diabetes and Digestive and Kidney Diseases. The aim of the network is to collect and analyze cases of severe liver injury caused by nonacetaminophen drugs and supplements.

In 2012, Dr. Navarro presented data comparing liver injuries related to bodybuilding drugs with those related to weight-loss drugs, as previously reported by *Medscape Medical News*.

In the current study, his group assessed the characteristics of liver injury related to bodybuilding supplements.

Dr. Navarro presented the results here at The Liver Meeting 2013.

The researchers found distinct differences in the characteristics of liver injury related to supplements and those related to prescription drugs.

Bodybuilding supplements are the most likely of all supplements to be related to liver injury. However, liver injuries related to bodybuilding supplements are generally less severe than those related to from prescription drugs.

Bodybuilders are not the only users of supplements. "We know that some 50% of the US population uses dietary supplements, so half of all patients seeing physicians might very well be using them. The physician has to ask," Dr. Navarro said.

Growing Popularity of Supplements

Determining the cause of supplement-induced liver toxicity is complicated by the fact that these products aren't regulated the way prescription drugs are, explained session comoderator Mary Rinella, MD, from Northwestern University in Chicago. Often what's in the bottle isn't what the label says, she pointed out.

Dr. Rinella cited a recent study that showed that products can be contaminated or substituted with alternative plant species and fillers, such as rice or wheat, which are not listed on the label (*BMC Med*. 2013;11:222).

"The bottom line is that it's not regulated and we don't know what's in the products," she said.

Patients enrolled in the network experienced liver injury in the previous 6 months They are evaluated at baseline and at 6 months and, if liver disease is ongoing, at 12 and 24 months. When possible, the supplement used by the patient is photographed, and aliquots are stored and analyzed.

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The researchers evaluated 845 cases of hepatotoxicity. Of these, 16% were deemed to be related to 1 or more supplement. The other 84% were related to prescription drugs.

Of the 262 supplements consumed by the 136 patients, 30% were marketed as bodybuilding products.

Bodybuilding supplements were used by 44 patients and other supplements were used by 85 patients. A combination of bodybuilding and other supplements was used by 7 patients; these were excluded from the analysis.

The proportion of patients with liver toxicity related to bodybuilding supplements increased from 2% in 2004 to 5% in 2013 (P = .01), and for other supplements increased from 5% in 2004 to 10% in 2013 (P = . 05).

Table. Characteristics of Patients by Cause of Liver Injury*

Characteristic	Bodybuilding Supplements	Other Supplements	Prescription Drugs
Mean age, y	33	48	50
Male, %	100	35	37
Mean weight, kg	87	75	77
Major comorbidities, %	21	52	69
Jaundice, %	100	78	68
Pruritus, %	84	48	53
Levels at hepatotoxicity onset			
Alanine aminotransferase, U/L	173	1019	505
Alkaline phosphatase, U/L	111	213	222
Total bilirubin, mg/dL	9.8	7.9	4.3
*P < .001 for all			

The median number of days until return to normal total bilirubin levels was significantly greater with bodybuilding supplements than with other supplements or prescription drugs (91 vs 44 vs 35 days; $P < .001$). However, there was no significant difference among the groups for return to normal alanine aminotransferase or alkaline phosphatase levels.

There was a trend toward longer median latency — defined as the number of days from start of the drug or supplement to the onset of liver injury — with bodybuilding supplements than with other supplements or prescription drugs, but this did not reach statistical significance (52 vs 38 vs 34 days; $P = .27$).

"Bodybuilding supplements produced a distinct presentation with prolonged jaundice. Injury from other supplements was more hepatocellular," Dr. Navarro noted.

Rates of hospitalization and all-cause mortality did not differ significantly in the 3 groups, but liver transplantation rates did. None of the patients in the bodybuilding supplement group underwent liver transplantation, whereas 13% of those in the other supplement group and 3% in the prescription drug group did ($P < .001$).

What Are They Taking?

Dr. Rinella said she routinely asks patients with liver injury what they're taking, and specifically asks about teas and any product purchased at a health-food store. "The public still doesn't believe how dangerous they can be," she told *Medscape Medical News.*

The fact that supplements might not even contain the ingredients they say they contain makes it much harder to determine the actual cause of liver injury, she noted. "You can't blame liver injury on St. John's wort when St. John's wort isn't even in the bottle."

And some of the fillers that are in the bottles can be hepatotoxic, too. "It's kind of scary. It's interesting that the Drug-Induced Liver Injury Network banked aliquots of drugs and will hopefully analyze them," Dr. Rinella told *Medscape Medical News*.

Dr. Navarro has disclosed no relevant financial relationships. Dr. Rinella serves on advisory boards for Gilead, Gore, and Genentech.

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